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Quarterly Progress Report Number 5

Transcutaneous Analyte Measuring Methods
(TAMM Phase II)

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Biotronics Technologies, Inc.

October, November, December, 1992

Naval Medical Research and Development Command

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(TAMM Phase II)

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Abstract

The major objectives of this quarter were to complete data collection at Froedtert Lutheran Memorial Hospital, to select and develop final TAMM algorithms for system redelivery to Bethesda NNMC and to establish the specifications for the final field instrument design.

Data collection at Froedtert was halted on December 4, 1992 after 193 patients. Improved techniques will be used for the collection of the remainder of data from patients at Froedtert.

An in-depth study of the 442-patient database has taken place throughout the quarter. Database irregularities were discovered and corrected. Algorithms were selected and are under development for the redelivery of an instrument to Bethesda and for the field instrument.

A schedule has been prepared for the Bethesda redelivery, the field instrument final design and the field instrument development and testing. The Bethesda shipment is scheduled for February 19, 1993. Field instrument design will be complete on March 18, 1993. Field instrument shipment is scheduled for April 30, 1993.

Data Collection

A number of data collection irregularities have come to light during data analysis. Three of the patient files were recorded with zero reference spectral values. These files do contain light intensity values and may be of some use, but absorbance calculations are impossible without reference spectra.

Five of the Froedtert patient files had duplicate names assigned by faulty data collection software. The detailed scan data were lost for these patients; however, the summary data is intact and can be used for some analysis. These eight patient files are not counted in the total given above.

From June 23, 1992 to July 1, 1992, 126 patient files were recorded at Bethesda NNMC using a 100-millisecond array integration time period. Data collection was suspended until July 21, 1992 to add patient temperature to the data collected and to fix a problem with patient race recording. When the updated software was reinstalled at Bethesda it reverted to the default value of 60 milliseconds for array integration time period. The remaining 123 patient files taken at Bethesda and all 193 files taken at Froedtert were recorded using the 60-millisecond array integration time period.

On October 23, 1992, after recording 119 patient files at Froedtert, data collection was suspended. On October 28, 1992 data collection was reinitiated with improved data collection techniques. The wrist and inside wrist positions that had performed poorly in previous analyses were replaced with second readings of the forearm and neck positions. The use of 9 blocks of 10 scans of light spectra interlaced with 9 blocks of 10 scans of dark spectra was replaced by 1 block of 90 scans of light spectra followed by 1 block of 90 scans of dark spectra. A low reflectance standard reading was added so that all patient files would contain both high and low reflectance standard spectra readings. Data collection continued at Froedtert until December 4, 1992, producing 72 additional patient files.

Data collection was reinitiated at Froedtert on January 13, 1993 using an array integration time period of 200 milliseconds. With these comments in mind, the data can be subdivided into 5 subsets using the following array integration times and light and dark spectra block sizes:

Data Subset	Hospital	Start Date	Stop Date	Integration Time Structure	Blocks of Scans	No.
1	Bethesda	6/23/92	7/01/92	100	9 of 10	124
2	Bethesda	7/21/92	8/05/92	60	9 of 10	126
3	Froedtert	9/09/92	10/23/92	60	9 of 10	119
4	Froedtert	10/28/92	12/04/92	60	1 of 90	79
* 5	Froedtert	1/13/93	1/27/93	200	1 of 90	100

* predicted

Data Analysis - Preprocessing Algorithms

Data analysis techniques used on the TAMM patient files include preprocessing algorithms and pattern recognition algorithms. Preprocessing algorithms manipulate the raw patient files eliminating noise before the pattern recognition algorithms are applied.

Patient files include 90 light spectra and 90 dark spectra taken of the patient's wrist, inside wrist, forearm and neck as well as a calibration standard and a high reflective standard. These 1080 spectra are recorded in 6 binary files. Twelve ASCII files are also recorded, one average light spectra and one average dark spectra, for each patient's positions and standards.

A number of preprocessing algorithms have been applied to the patient data base. They include the following:

a. Subtracting the average dark spectra from the average light spectra;

b. Dividing the average light minus dark position spectra by the average light minus dark standard spectra;

c. Calculating absorbance;

d. Calculating smoothed absorbance;

e. Calculating smoothed absorbance with a single wavelength reference;

f. Calculating the first derivative of absorbance;

g. Calculating the smoothed first derivative of absorbance;

h. Calculating the normalized first derivative of absorbance;

i. Using an adaptive filter to remove all dark spectra correlated information from light spectra;

j. Using an adaptive filter to remove all high reference light standard spectra correlated information from light spectra; and

k. High/low T-value (tracking value) analyte/wavelength sensitivity analysis.

Data Analysis - Pattern Recognition Algorithms

Pattern recognition algorithms use preprocessed patient files as inputs for estimating patient blood analyte concentrations.

The pattern recognition algorithms evaluated on the TAMM patient data include the following:

a. Stepwise multi-variable regression analysis;

b. Rotated principal component regression analysis;

c. Adaptive filter analysis; and

d. Neural network and genetic algorithm analysis (NETGEN).

Results

Of all the combinations of preprocessing and pattern recognition algorithms that were tried on the TAMM patient data, the best results to date were produced as follows:

a. Subtracting the average dark spectra from the average light spectra;

b. Dividing the average light minus dark position spectra by the average light minus dark standard spectra;

c. Calculating the normalized first derivative of absorbance; and

d. Neural network and genetic algorithm analysis (NETGEN).

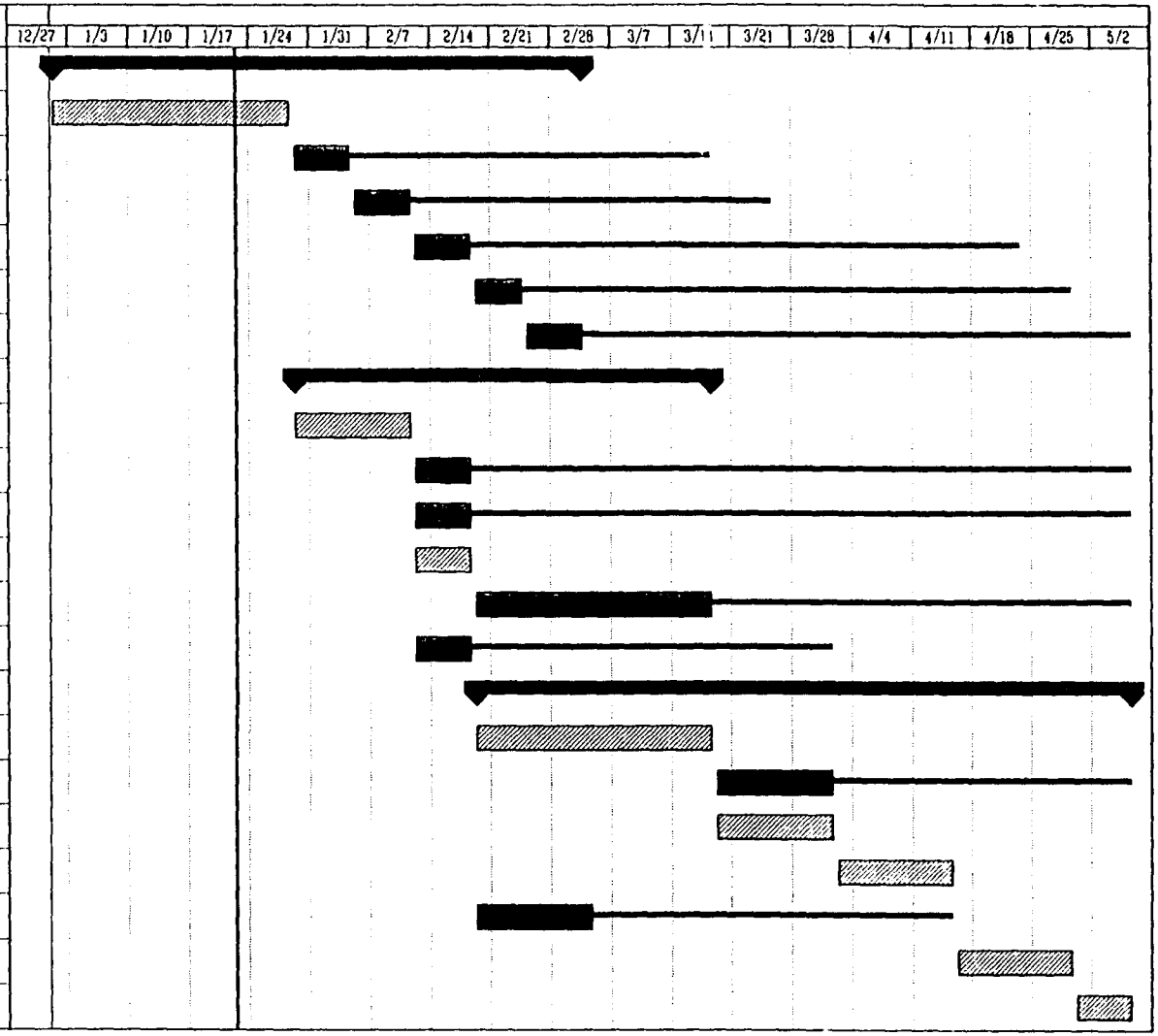
Delivery Schedule

A detailed delivery schedule is provided in Figure 1. The instrument is in deliverable condition now except for software. Preprocessing and analytical software will be written and tested on the instrument by February 19, 1993. The instrument will be shipped immediately. Field instrument design will begin on January 29 and will be completed by February 19. Then field instrument development will be initiated and will be completed by April 29, 1993.

Kenneth J. Schlager
Principal Investigator

Bruce H. Boehlen
Project Manager

ID	Name	Prede.	Scheduled Start	Scheduled Finish	Duration
1	BETHESDA 800		1/1/93	3/3/93	8.77ew
2	ANALYSIS EVALUATION		1/1/93	1/28/93	4w
3	PREPROCESSING SOFTWARE	2	1/29/93	2/4/93	1w
4	ANALYTICAL SOFTWARE	3	2/5/93	2/11/93	1w
5	INTEGRATE/TEST	4	2/12/93	2/18/93	1w
6	SHIP	5	2/19/93	2/24/93	0.8w
7	TRAIN	6	2/25/93	3/3/93	1w
8	FIELD INSTRUMENT DESIGN		1/29/93	3/18/93	6.91ew
9	OPTICAL PATH	2	1/29/93	2/11/93	2w
10	ELECTRONICS/POWER	9	2/12/93	2/18/93	1w
11	COMPONENT SELECTION/ORDER	9	2/12/93	2/18/93	1w
12	ENVIRONMENTAL DESIGN	9	2/12/93	2/18/93	1w
13	PACKAGE DESIGN	12	2/19/93	3/18/93	4w
14	SOFTWARE DESIGN	4	2/12/93	2/18/93	1w
15	FIELD INSTRUMENT DEVELOPMENT		2/19/93	5/6/93	10.91ew
16	WAIT FOR PARTS	12	2/19/93	3/18/93	4w
17	OPTICAL ASSEMBLY/TEST	16	3/19/93	4/1/93	2w
18	ELECTRONICS ASSEMBLY/TEST	16	3/19/93	4/1/93	2w
19	ENCLOSURE ASSEMBLY/TEST	18	4/2/93	4/15/93	2w
20	SOFTWARE REWRITE	14	2/19/93	3/4/93	2w
21	INTEGRATION/TEST	19,20	4/16/93	4/29/93	2w
22	SHIP AND TRAIN	21	4/30/93	5/6/93	1w



Project: TAMM
Date: 1/22/93

Critical
Noncritical
Progress
Milestone
Summary
Slack

Figure 1.